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09/867,201	05/29/2001	Jen-i Mao	55525-8057	5899

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EXAMINER	
FREDMAN, JEFFREY NORMAN	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 04/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 10/03)

Office Action Summary	Application No. 09/867,201	Applicant(s) MAO ET AL.
	Examiner Jeffrey Fredman	Art Unit 1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/6/01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1-14 in the reply filed on February 27, 2006 is acknowledged.

Claim Interpretation

2. The second step of claim 1 incorporates the limitation "each polynucleotide fragment of the same size ladder having an end and the same oligonucleotide tag as every other polynucleotide fragment of the size ladder". iThe first requirement, that the polynucleotide have an "end" is clear. The second requirement, that "each polynucleotide fragment" has the "same oligonucleotide tag as every other polynucleotide fragment" is less so. Since step a) requires that every polynucleotide have a different oligonucleotide tag attached, the second requirement may simply be a reiteration of this requirement. Alternatively, this may indicate an implicit requirement for a step of cloning or otherwise replicating the tagged molecules so that there are multiple identical copies of each polynucleotide.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1, 4, 6-8 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Wong (U.S. Patent 5,935,793).

Wong teaches a method of claims 1 and 6 of sequence determination (see abstract) comprising:

(a) attaching an oligonucleotide tag from a repertoire of tags to each polynucleotide of the population to form tag-polynucleotide conjugates such that substantially every different polynucleotide has a different oligonucleotide tag attached (see column 7, lines 45-61, which teaches "'identifier tags', which are used to uniquely identify the sample fragment or template to which each tag is attached" and see column 25, claim 1, step b where tags are attached),

(b) generating a size ladder of polynucleotide fragments for each tag-polynucleotide conjugate, each polynucleotide fragment of the same size ladder having an end and the same oligonucleotide tag as every other polynucleotide fragment of the size ladder (see column 11, line 43 to column 12, line 64, where sequencing fragments are generated, also see column 26, claim 1, substeps 3-5 of step (b)) (also related to the second interpretation in the claim interpretation section, see column 10, where Wong teaches cloning the polynucleotides into a vector to create multiple copies of the polynucleotide),

(c) separating the polynucleotide fragments into size classes (see column 17, line 20 to column 18, line 59 and see column 26, claim 1, step (c)),

(d) labeling the polynucleotide accoridng to the identity of one or more nucleotides at the end of such polynucleotide fragment (see column 19, lines 58-63, column 17, lines 10-35, column 14, lines 35-45, and column 27, claim 9, where "a different fluorescent label is used to identify each different terminating base type"),

(e) copying the labeled oligonucleotide tags of each polynucleotide fragment of each size class (see column 18, line 60 to column 19, line 31, where the isolated sequencing fragments are amplified by PCR, also see column 26, claim 1, step (e)),

(f) separately hybridizing the labeled oligonucleotide tags of each size class with their respective complements under stringent hybridization conditions, the respective complements being attached as populations of substantially identical oligonucleotides in spatially discrete and addressable regions on one or more solid phase supports and the respective signature sequences being determined by the sequence of labels associated with each spatially discrete and addressable region of the one or more solid phase supports (see column 19, line 50 to column 20, line 46 and column 26, claim 1, steps (f) and (g)).

With regard to claim 4, Wong teaches forming extension products of known length for each tag-polynucleotide (see column 11, line 43 to column 12, line 64, where sequencing fragments are generated).

With regard to claim 7, Wong teaches formation of a size ladder for each tag-polynucleotide (see column 17, line 20 to column 18, line 59 and see column 26, claim 1, step (c)).

With regard to claims 8, 10, Wong teaches physical separation using electrophoretic methods such as gel electrophoresis (see column 18, lines 1-37, for example).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-12 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brenner (U.S. Patent 5,763,175) in view of Wong (U.S. Patent 5,935,793).

Brenner teaches a method of sequence determination (see abstract) comprising:

(a) attaching an oligonucleotide tag from a repertoire of tags to each polynucleotide of the population to form tag-polynucleotide conjugates such that substantially every different polynucleotide has a different oligonucleotide tag attached (see column 2, lines 43-46, which teaches "An important aspect of my invention is the attachment of an oligonucleotide tag to each polynucleotide of a population such that substantially all different polynucleotides have different tags" and see column 20),

(b_1) generating a size ladder of polynucleotide fragments for each tag-polynucleotide conjugate, each polynucleotide fragment of the same size ladder having an end and the same oligonucleotide tag as every other polynucleotide fragment of the size ladder (see column 21, lines 29-37, where BbvI cleaves the tag-polynucleotide conjugate to form size ladders)

(b_2) wherein the generating step operates by shortening by a different amount said polynucleotides of said tag-polynucleotide conjugates in each aliquot such that said polynucleotides are shortened by a different amount (see column 21, lines 29-45, where the type IIs enzyme BbvI is used to shorten),

(b3) wherein extension products of known length are ligated onto each tag-polynucleotide (see column 21, lines 38-45, where S primers are ligated to the cleaved tag-conjugates).

(d) labeling the polynucleotide according to the identity of one or more nucleotides at the end of such polynucleotide fragment (see column 21, lines 20-25, where the polynucleotide is labeled),

(e) copying the labeled oligonucleotide tags of each polynucleotide fragment of each size class (see column 18, line 60 to column 19, line 31, where the isolated sequencing fragments are amplified by PCR, also see column 26, claim 1, step (e)),

(f) separately hybridizing the labeled oligonucleotide tags of each size class with their respective complements under stringent hybridization conditions, the respective complements being attached as populations of substantially identical oligonucleotides in spatially discrete and addressable regions on one or more solid

phase supports and the respective signature sequences being determined by the sequence of labels associated with each spatially discrete and addressable region of the one or more solid phase supports (see column 19, line 50 to column 20, line 46 and column 26, claim 1, steps (f) and (g)).

With regard to claims 2-3, 9, Brenner teaches where the type IIs enzyme BbvI is used to shorten (see column 21, lines 29-45).

With regard to claims 4-5, Brenner teaches wherein extension products of known length are ligated onto each tag-polynucleotide (see column 21, lines 38-45, where S primers are ligated to the cleaved tag-conjugates).

With regard to claims 11-12, Brenner teaches extension oligonucleotides of about 12 nucleotides (see column 13, line 13).

With regard to claim 14, Brenner teaches the use of inosine (see column 20, lines 1-10).

Brenner does not expressly teach a step of generating a size ladder and separating the polynucleotide into size classes.

Wong teaches a method of claims 1 and 6 of sequence determination (see abstract) comprising:

(a) attaching an oligonucleotide tag from a repertoire of tags to each polynucleotide of the population to form tag-polynucleotide conjugates such that substantially every different polynucleotide has a different oligonucleotide tag attached (see column 7, lines 45-61, which teaches "'identifier tags', which are used to uniquely identify the sample fragment or template to which each tag is attached" and see column

25, claim 1, step b where tags are attached),

(b) generating a size ladder of polynucleotide fragments for each tag-polynucleotide conjugate, each polynucleotide fragment of the same size ladder having an end and the same oligonucleotide tag as every other polynucleotide fragment of the size ladder (see column 11, line 43 to column 12, line 64, where sequencing fragments are generated, also see column 26, claim 1, substeps 3-5 of step (b)) (also related to the second interpretation in the claim interpretation section, see column 10, where Wong teaches cloning the polynucleotides into a vector to create multiple copies of the polynucleotide),

(c) separating the polynucleotide fragments into size classes (see column 17, line 20 to column 18, line 59 and see column 26, claim 1, step (c)),

(d) labeling the polynucleotide accoridng to the identity of one or more nucleotides at the end of such polynucleotide fragment (see column 19, lines 58-63, column 17, lines 10-35, column 14, lines 35-45, and column 27, claim 9, where "a different fluorescent label is used to identify each different terminating base type"),

(e) copying the labeled oligonucleotide tags of each polynucleotide fragment of each size class (see column 18, line 60 to column 19, line 31, where the isolated sequencing fragments are amplified by PCR, also see column 26, claim 1, step (e)),

(f) separately hybridizing the labeled oligonucleotide tags of each size class with their respective complements under stringent hybridization conditions, the respective complements being attached as populations of substantially identical oligonucleotides in spatially discrete and addressable regions on one or more solid

phase supports and the respective signature sequences being determined by the sequence of labels associated with each spatially discrete and addressable region of the one or more solid phase supports (see column 19, line 50 to column 20, line 46 and column 26, claim 1, steps (f) and (g)).

With regard to claim 4, Wong teaches forming extension products of known length for each tag-polynucleotide (see column 11, line 43 to column 12, line 64, where sequencing fragments are generated).

With regard to claim 7, Wong teaches formation of a size ladder for each tag-polynucleotide (see column 17, line 20 to column 18, line 59 and see column 26, claim 1, step (c)).

With regard to claims 8, 10, Wong teaches physical separation using electrophoretic methods such as gel electrophoresis (see column 18, lines 1-37, for example).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify Brenner to incorporate the size separation as taught by Wong since Wong teaches "Conveniently, the sample or samples contain polynucleotide fragments within a selected size range, e.g., 400-2000 nucleotides, to achieve a desired sampling frequency for effective shotgun sequencing (see column 12, lines 6-16)."

The ordinary practitioner would have been motivated by Brenner to select a particular sampling frequency since Brenner wishes to avoid doubles and Brenner notes that

"Thus, a design tradeoff exists between selected a large sample of target polynucleotides – which, for example, ensures adequate coverage of a target polynucleotide in a shotgun seuqencing operation and selecting a small sample which ensures that a minimal number of doubles will be present (see column 11, lines 50-55)." An ordinary practitioner would therefore have been motivated to modify Brenner, who is interested in selecting the correct amount of polynucleotide for shotgun seuqencing, by using the size selection of Wong to achieve a sampling frequency expressly discussed by Wong as useful for shotgun sequencing.

8. Claims 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Brenner (U.S. Patent 5,763,175) in view of Wong (U.S. Patent 5,935,793) and further in view of Strathmann (U.S. Patent 6,480,791).

Brenner in view of Wong teach the limitations of claims 1-12 and 14 as discussed above.

Brenner in view of Wong do not teach the use of HPLC.

Wong does teach that "The size range may be controlled further by subjecting the sample to agarose, or polyacrylamide gel electrophoresis, size-exclusion chromatography, or other separation methods (see column 12, lines 12-15)."

Strathmann teaches that tagged polynucleotides can be separated by HPLC as a known equivalent chromatography method (see column 29, lines 25-64).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize HPLC separation in the method of Brenner in

view of Wong since Strathman teaches that HPLC is an known equivalent method which will function to separate the tagged nucleic acids by size and since MPEP 2144.06 notes " Substituting equivalents known for the same purpose. In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. In re Fout , 675 F.2d 297, 213 USPQ 532 (CCPA 1982)."

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jeffrey Fredman
Primary Examiner
Art Unit 1637
3/24/05